Macaque sp|P15568|APA1_MACFA Apolipoprotein A-I precursor (Apo-AI) - Macaca fascicularis (Crab eating macaque) (SEQ ID NO:16).

Bovine sp|P15497|APA1_BOVIN Apolipoprotein A-I precursor (Apo-AI) - Bos taurus (Bovine) (SEQ ID NO:17).

Pig sp|P18648|APA1_PIG Apolipoprotein A-I precursor (Apo-AI) - Sus scrofa (Pig) (SEQ ID NO:18).

Dog sp|P02648|APA1_CANFA Apolipoprotein A-I precursor (Apo-AI) - Canis familiaris (Dog) (SEQ ID NO:19).

Rabbit sp|P09809|APA1_RABIT Apolipoprotein A-I precursor (Apo-AI) - Oryctolagus cuniculus (Rabbit) (SEQ ID NO:20).

Tree shreew sp|O18759|APA1_TUPGB Apolipoprotein A-I precursor (Apo-AI) - Tupaia glis belangeri (Common tree shrew) (SEQ ID NO:21).

Mouse sp|Q00623|APA1_MOUSE Apolipoprotein A-I precursor (Apo-AI) - Mus musculus (Mouse) (SEQ ID NO:22).

Rat sp|P04639|APA1_RAT Apolipoprotein A-I precursor (Apo-AI) - Rattus norvegicus (Rat) (SEQ ID NO:23).

Eur. Hedgehog tr|Q9TS49 APOLIPOPROTEIN A-I, APOA-I=CHOLESTEROL TRANSPORTER - Erinaceus europaeus (Western European hedgehog) (SEQ ID NO:24).

Chicken sp|P08250|APA1_CHICK Apolipoprotein A-I precursor (Apo-AI) - Gallus gallus (Chicken) (SEQ ID NO:25).

Jap. quail sp|P32918|APA1_COTJA Apolipoprotein A-I precursor (Apo-AI) - Coturnix coturnix japonica (Japanese quail) (SEQ ID NO:26).

Domestic duck sp|O42296|APA1_ANAPL Apolipoprotein A-I precursor (Apo-AI) - Anas platyrhynchos (Domestic duck) (SEQ ID NO:27).

Rainbow trout sp|O57523|AP11_ONCMY Apolipoprotein A-I-1 precursor (APOA-I-1) - Oncorhynchus mykiss (Rainbow trout) (Salmo gairdneri) (SEQ ID NO:28).

Brown trout sp|Q91488|APA1_SALTR Apolipoprotein A-I precursor (Apo-AI) - Salmo trutta (Brown trout) (SEQ ID NO:29).

Atl. salmon sp|P27007|APA1_SALSA Apolipoprotein A-I precursor (Apo-AI) - Salmo salar (Atlantic salmon) (SEQ ID NO:30).

Zebrafish sp|O42363|APA1_BRARE Apolipoprotein A-I precursor (Apo-AI) - Brachydanio rerio (Zebrafish) (Zebra danio) (SEQ ID NO:31).

Sea bream sp|O42175|APA1_SPAAU Apolipoprotein A-I precursor (Apo-AI) - Sparus aurata (Gilthead sea bream) (SEQ ID NO:32).

Figure 2B shows aligned amino acid sequences (in one letter code) for human (SEQ ID NO:33), macaque (SEQ ID NO:34), mouse (SEQ ID NO:35), baboon (SEQ ID NO:36), pig (SEQ ID NO:37), and rat (SEQ ID NO:38) apolipoprotein A-IV.--

Please amend the 7 paragraphs beginning at line 11 of page 9 and ending at line 15 of page 10 with the following rewritten 7 paragraphs:

--Figure 4 shows an alignment of the amino acid sequences of the trimerising structural element of the tetranectin protein family. Amino acid sequences (one letter code) corresponding to residue V17 to K52 comprising exon 2 and the first three residues of exon 3 of human tetranectin (SEQ ID NO:39); murine tetranectin (SEQ ID NO:40) (Sørensen et al., Gene, 152: 243 -245, 1995); tetranectin homologous protein isolated from reefshark cartilage (SEQ ID NO:42) (Neame and Boynton, 1992,1996); and tetranectin homologous protein isolated from bovine cartilage (SEQ ID NO:41) (Neame and Boynton, database accession number PATCHX:u22298). Residues at a and d positions in the heptad repeats are listed in boldface. The listed consensus sequence of the tetranectin protein family trimerising structural element comprise the residues present at a and d positions in the heptad repeats shown in the figure in addition to the other conserved residues of the region. "hy" denotes an aliphatic hydrophobic residue.

Figure 5 shows the pT7 H6UbiFx Apo A-I plasmid (SEQ ID NO:43) and its corresponding amino acid sequence (SEQ ID NO:44). The expressed and processed polypeptide consists of

amino acids no 25-267 from human Apo A-I (SEQ ID NO 1) and gly-gly linked N-terminally thereto.

Figure 6 shows the pT7 H6UbiFx Cys-Apo A-I plasmid (SEQ ID NO:45) and its corresponding amino acid sequence (SEQ ID NO:46). The expressed and processed polypeptide consists of a N-terminal cystein residue and the amino acids no 25-267 from human Apo A-I (SEQ ID NO 2) and gly-gly linked N-terminally thereto.

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Figure 7 shows the pT7H6 Trip-A-Apo A-I - Amp^R plasmid (SEQ ID NO:47) and its corresponding amino acid sequence (SEQ ID NO:48). The expressed and processed polypeptide (SEQ ID NO 3) consists of the tetranectin trimerising structural element (TTSE), a linking sequence, and amino acids no 25-267 from human Apo A-I.

Figure 8 shows the pT7H6 Trip-A-Apo A-I-del 43 - Amp^R plasmid (SEQ ID NO:49) and its corresponding amino acid sequence (SEQ ID NO:50). The expressed and processed polypeptide (SEQ ID NO 4) consists of the TTSE, a linking sequence, and amino acids no 68-267 from human Apo A-I.

Figure 9 shows the pT7H6FXCysApoAI plasmid (SEQ ID NO:51) and its corresponding amino acid sequence (SEQ ID NO:52). The expressed and processed polypeptide consists of a N-terminal cystein residue and the amino acids no 25-267 from human Apo A-I (SEQ ID NO 2) and gly-gly linked N-terminally thereto.

Amend

Figure 10 A to G shows illustrative examples of plasmids (SEQ ID NOs:53, 55, 57, 59, 61, 63 and 65, respectively) and corresponding amino acid sequences (SEQ ID NOs:54, 56, 58, 60, 62, 64 and 66, respectively) for apolipoprotein constructs according to the present invention.--

Please amend the paragraph beginning at line 23 of page 11 with the following rewritten paragraph:

--Fig 10 H: pT7H6Fx-Hp(alpha)-ApoAI. The plasmid (SEQ ID NO:67) codes for the fusion protein (SEQ ID NO:68) between Hp(alpha) and ApoAi. The mature protein product is called Hp(alpha)-ApoAI (SEQ ID NO 14).--

Amend

Please amend the four paragraphs beginning at line 17 of page 27 and ending at line 19 of page 28 with the following rewritten four paragraphs:

--**Tetranectin based linker:**

The linker may include the tetranectin residues 53-56, which in tetranectin forms a β-strand, and the residues 57-59 which forms a turn in tetranectin (Nielsen BB, Kastrup JS, Rasmussen H, Holtet TL, Graversen JH, Etzerodt M, Thøgersen HC, Larsen IK, FEBS-Letter 412, 388-396, 1997). The sequence of the segment is GTKVHMK (SEQ ID NO:69). This linker has the advantage that it in native tetranectin is bridging the trimerisation domain with the CRD-domain, and

hence is imagined to be well suited for connecting the trimerisation domain to another domain in general. Furthermore the resulting construct is not expected to be more immunogenic than the construct without a linker. The tetranectin based linker is highly preferred when the component X comprises the TTSE.

Fibronectin based linker:

The linker may be chosen as a sub-sequence from the connecting strand 3 from human fibronectin, this corresponds to amino acid residues 1992-2102 (SWISS-PROT numbering, entry P02751). Preferably the subsequence: PGTSGQQPSVGQQ (SEQ ID NO:70) covering amino acid residues number 2037-2049 is used, and within that subsequence the segment GTSGQ (residues 2-6 of SEQ ID NO:70) corresponding to amino acid residues 2038-2042 is more preferable. This construct has the advantage that it is know not to be highly prone to proteolytic cleavage and is not expected to be highly immunogenic bearing in mind that fibronectin is present at high concentrations in plasma.

Human IgG_3 upper hinge based linker

The 10 amino acid residue sequence derived from the upper hinge region of murine IgG_3, PKPSTPPGSS (SEQ ID NO:71), has been used for the production of antibodies dimerised trough a coiled coil (Pack P. and Plückthun, A. Biochemistry **31**, pp 1579-1584 (1992)) and may be useful as a spacer peptide according to the present invention. Even more preferable may

be a corresponding sequence from the upper hinge region of human IgG_3. Sequences from human IgG_3 are not expected to be immunogenic in human beings.

Flexible linkers

Possible examples of flexible linker/spacer sequences include SGGTSGSTSGTGST (SEQ ID NO:72), AGSSTGSSTGPGSTT (SEQ ID NO:73) or GGSGGAP (SEQ ID NO:74). These sequences have been used for the linking of designed coiled coils to other protein domains (Müller, K. M., Arndt, K. M. and Alber, T., Meth. Enzymology, **328**, pp 261-281 (2000).

Please amend the paragraph beginning at line 14 of page 41 with the following rewritten paragraph:

The cDNA encoding Apo A-I was amplified from a human liver cDNA library (Clontech) using standard PCR techniques. For the construction of Ubi-A-I the primers used were: 5′-CAC GGA TCC ATC GAG GGT AGG GGT GGA GAT GAA CCC CCC CAG AGC-3′ (SEQ ID NO:75) and 5′- TCC AAG CTT ATT ACT GGG TGT TGA GCT TCT TAG TG-3′ (SEQ ID NO:76). The product was cloned into the vector pT7H6Ubi, described in (Ellgaard L. et al Eur. J. Biochem. 1997;244(2):544-51) using the Bam HI and Hind III cloning sites. For the construction of Trip-A-A-I the primers used were 5′-AAG GGA TCC GAT GAA CCC CCC CAG AGC CCC-3′ (SEQ ID NO:77) and 5′-TCC AAG CTT ATT ACT GGG TGT TGA GCT TCT TAG

TG-3′ (SEQ ID NO:78). The PCR product was cloned into the pT7H6tripa vector described in WO 98/56906 using the Bam HI and Hind III cloning sites. For the construction of Trip-A-I-del43 the primers used were 5′-AGG GGA TCC CTA AAG CTC CTT GAC AAC TGG G-3′ (SEQ ID NO:79) and 5′- TCC AAG CTT ATT ACT GGG TGT TGA GCT TCT TAG TG -3′ (SEQ ID NO:80). The PCR product was cloned into the pT7H6tripa vector described in WO 98/56906 using the Bam HI and Hind III cloning sites. For the construction of Ubi-Cys-A-I the primers used were: 5′-GGT GGA TCC ATC GAG GGT AGG GGT GGA TGT GAT GAA CCC CCC C -3′ (SEQ ID NO:81) and 5′- TCC AAG CTT ATT ACT GGG TGT TGA GCT TCT TAG TG -3′ (SEQ ID NO:82). The product was cloned inti the vector pT7H6Ubi, described in (Ellgaard L. et al Eur. J. Biochem. 1997;244(2):544-51) using the Bam HI and Hind III cloning sites. The plasmids generated are shown on figure 4, 5, 6, and 7.

Please amend the paragraphs beginning at line 34 of page 46 and ending at line 17 of page 47 with the following rewritten paragraphs:

--pT7H6FX-Trip-A-FN(-2)-AI:

5′-CGC GGATCC TCG GGT CAG GAT GAA CCC CCC CAG AGC CCC -3′ (SEQ ID NO:83)

Unfortunately all the isolated clones had the above highlighted **G** mutated to a T, indicating a faulty sequence of the primer.

pT7H6FX-Trip-A-TN-AI-Bam-S

5′- cgc gga tcc aag gtg cac atg aag gat gaa ccc ccc cag agc ccc-3′ (SEQ ID NO:84)

The mutations mentioned was corrected by site directed mutagenesis using the QuickChange kit from Stratagene and the following sets of primers:

pT7H6FX-Trip-FN-AI:

5′-acg gtc tcc ctg aag gga acc tcg ggt cag gat g-3′ (SEQ ID NO:85)

5′-cat cct gac ccg agg ttc cct tca ggg aga ccg t-3′

pT7H6FX-Trip-A-TN-AI

5′-acg gtc tcc ctg aag gga acc aag gtg cac atg aag g-3′ (SEQ ID NO:86)

5′-cct tca tgt gca cct tgg ttc cct tca ggg aga ccg t-3′

Please amend the paragraphs beginning at line 26 of page 47 and ending at line 33 of page 47 with the following rewritten paragraphs:

--The paragraphs beginning at line 26 of page 47 and ending at line 33 of page 47 have been amended as follows:

For the mutation of lysine 9 from Trip-A: